IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ILLINOIS
EASTERN DIVISION

UNIONDALE CHEMISTS, INC., on behalf of itself and all others similarly situated,	)	No.
Plaintiff,	)	JURY TRIAL DEMANDED
v.	)	
ASTELLAS PHARMA US, INC.,	)	
Defendant.	)	

CLASS ACTION COMPLAINT

Plaintiff, Uniondale Chemists, Inc. ("Plaintiff"), individually and on behalf of a class of all direct purchasers similarly situated, brings this action for damages, treble damages, injunctive relief and costs of this suit under the antitrust laws of the United States against Astellas Pharma US, Inc. ("Astellas" and/or "Defendant"), and alleges as follows based on (a) personal knowledge as to matters relating to Plaintiff, (b) the investigation of Plaintiff's counsel, including review of Defendant's citizen petitions and other filings with the United States Food and Drug Administration ("the FDA"), and filed court papers and court opinions regarding Defendant's motions for Temporary Restraining Order and Preliminary Injunction; and (c) information and belief as to all other matters:

INTRODUCTION

1. This case arises out of Defendant's unlawful attempt to manipulate the regulatory process for the approval of generic version of tacrolimus, an immunosuppressant approved to help prevent organ rejection in patients who have received organ transplants. Defendant

manufactures Prograf, an FDA approved branded version of tacrolimus, which for years has been the sole source for this critical life-saving drug.

2. Faced with a potential competitive threat, Astellas engaged in a campaign to fraudulently delay the introduction of cheaper generic versions of Prograf, by abusing and manipulating the regulatory process to unlawfully extend its monopoly over the tacrolimus market. Astellas' motive for foreclosing generic entry to this market was to keep its monopoly position in the $920 million a year tacrolimus market.

3. As a result of its anticompetitive conduct to keep generic versions of Prograf off the market and in violation of §2 of the Sherman Act, Astellas: (a) illegally maintained monopoly power in the market for tacrolimus in the United States for up to twenty-three months; (b) maintained the price of Prograf at supra-competitive levels; and (c) overcharged Uniondale Chemists and members of the proposed class of direct purchasers of tacrolimus millions of dollars by depriving them of the benefits of unrestricted competition and access to cheaper generic versions of tacrolimus.

I. JURISDICTION AND VENUE

4. The Court has subject matter jurisdiction under 28 U.S.C. §1331 and 1337, as this action arises under Section 2 of the Sherman Act, 15 U.S.C. § 2, and Section 4 and 16 of the Clayton Act, 15 U.S.C. § 15(a) and 26.

5. Venue is proper in this District because Defendant resides in this District and transacts substantial business in this District as provided in 28 U.S.C. § 1391 (b) and (c). Additionally, a substantial part of the interstate trade and commerce involved and affected by the alleged violations of the antitrust laws was and is carried on in part within this District.

6. The Court has personal jurisdiction over Defendant because it resides in this District. Defendant sold Prograf in this District and throughout the United States, and engaged in a fraudulent scheme to restrict competition in the market for tacrolimus that was directed at and had the intended effect of causing injury to persons and entities residing or located in or doing business in this District and throughout the United States.

II. PARTIES

7. Plaintiff, Uniondale Chemists is a retail pharmacy located in Uniondale, New York. Uniondale Chemists is the assignee of claims from a wholesaler which purchased Prograf directly from the Defendant during the class period.

8. Defendant, Astellas Pharma US, Inc., is a Delaware Corporation with its principal offices located at Three Parkway North, Deerfield, Illinois. Astellas Pharma US, Inc. is the US affiliate of Astellas Pharma Inc., Tokyo, Japan.

INTERSTATE TRADE AND COMMERCE

9. The Defendant's activities, as described in this Complaint, were within the flow of and substantially affected interstate commerce.

10. During the time period covered by this Complaint, Defendant marketed and sold Prograf continuously in interstate commerce to customers located throughout the United States.

11. Defendant has used instrumentalities of interstate commerce to market and sell Prograf to customers located throughout the United States.

12. Defendant's efforts to monopolize the market for tacrolimus had a direct, substantial, and reasonable foreseeable effect on interstate commerce.

III. BACKGROUND

A. Regulatory Process for Generic Drugs

13. The Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 301 *et seq.*, requires that a company receive FDA approval before it may begin selling a new drug. Pre-market approval for a new drug, often referred to as a "pioneer" or "branded" drug, must be sought by filing a New Drug Application ("NDA") with the FDA demonstrating that the drug is safe and effective for its intended use.

14. In addition to information on safety and efficacy, NDA applicants must submit to the FDA a list of all patents that claim the drug for which FDA approval is being sought, or that claim a method of using the drug, and with respect to which a claim of patent infringement could reasonably be asserted against an unlicensed manufacturer or seller of the drug.

15. Congress enacted the Drug Price Competition and Patent Term Restoration Act ("Hatch-Waxman Act") in 1984 to establish an abbreviated process to expedite and facilitate the development and approval of more affordable generic drugs, while still allowing new drug innovators to obtain an economic return on their investments and discoveries. To effectuate this purpose, the Hatch Waxman Act permits a generic drug manufacturer to file an "abbreviated" new drug application ("ANDA"), which incorporates by reference the safety and effectiveness data developed and previously submitted by the company that manufactured the original, "pioneer" drug. The Hatch-Waxman Act also provides an economic incentive to the generic companies to be the first to file an ANDA for a particular generic drug: a 180-day statutory period of market exclusivity, during which time the manufacturer has the right to market its drug free from other generic competition.

16. Section 505(j) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355(j)), allows a generic manufacturer to rely on the FDA's previous findings that the pioneer drug is

safe and effective. Under this process, an ANDA applicant must demonstrate that its drug is bioequivalent to the pioneer drug (505(j)(2)(A)(iv)). In addition, an ANDA must contain information to show that the proposed drug has the same active ingredient(s), indications for use, route of administration, dosage form, strength, and labeling as the pioneer (505(j)(2)(A).

17. FDA classifies as therapeutic equivalents those products that meet the following general criteria: (1) Approved as safe and effective; (2) Pharmaceutical equivalents; (3) Bioequivalent; (4) Adequately labeled; (5) and Manufactured in compliance with Current Good Manufacturing Practices regulations. Bioequivalence demonstrates that the active ingredient of the proposed generic drug would be present in the blood of a patient to the same extent and for the same amount of time as the branded drug. 21 U.S.C.§355(j)(8)(B).

18. The FDA considers two products bioequivalent if the 90% CI of the relative mean Cmax, AUC(0-t) and AUC(0-∞) of the test (e.g. generic formulation) to reference (e.g. innovator brand formulation) should be within 80.00% to 125.00% in the fasting state. Although there are a few exceptions, generally a bioequivalent comparison of Test to Reference formulations also requires administration after an appropriate meal at a specified time before taking the drug, a so-called "fed" or "food-effect" study. A food-effect study requires the same statistical evaluation as the fasting study, described above.

IV. The Introduction of Generic Drugs to the Market Take Significant Sales From Brand Name Drugs

19. Bioequivalent drugs receive an "AB" rating from the FDA, indicating they are therapeutically equivalent to other drugs with the same rating in the same category. Generic versions of brand name drugs, which are AB-rated are usually priced below their brand name counterparts. Because of the price differential, AB-rated generic versions are substituted for their brand name counterparts under various statutory schemes which allow pharmacists in most

states, to substitute an AB-rated generic version of a drug for the brand name drug without seeking or obtaining permission from the prescribing doctor.

20. Sandoz Inc.'s tacrolimus capsules are AB-rated generic versions of Astellas' Prograf, indicating the drugs are therapeutically equivalent and bioequivalent to one another. According to an Astellas expert, Heather Goodman, Esq., the most significant reasons why a generic tacrolimus would be substituted for Astelllas' pioneer tacrolimus product, Prograf, include that "the generic [version] is less expensive than the brand drug" and "third-party payors such as Medicare, Medicaid, private insurers, and pharmacy benefit managers ("PBM"), within a certain period of time after an FDA-approved generic drug became commercially available, generally decline to cover more than the generic price (or significantly reduce what they will pay). Patients demand generic products as a result. In addition, generic manufacturers provide significant financial incentives to sell, cover and/or dispense their particular generic."

A. Citizen Petitions to the FDA

21. Federal regulations governing the FDA allow any person or entity, including a, pharmaceutical company, to file a citizen petition with the FDA requesting that the FDA take or refrain from taking, any administrative action. 21 C.F.R. 10.30.

22. The citizen petition must contain not only a statement of what action is being requested, but also a justification for that action, including, if appropriate, convincing scientific data and other information. The submitter of the citizen petition must also include a certification stating that the petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the views expressed in the citizen petition.

23. Petitioners are required to disclose, under penalty of perjury, the date on which the information in the petition became known to them, and the names of any persons or organizations that paid the petitioner to complete or file the petition.

B. Manufacturers of Branded Products Use Citizen Petitions to Forestall Generic Competition

24. The FDA spends a substantial amount of time and resources in reviewing and responding to these citizen petitions. Although citizen petitions can provide an opportunity for individuals to express their genuine concerns about safety, scientific, or legal issues regarding a product anytime before its market entry, and often make legitimate challenges, the reality is that brand-name pharmaceutical companies have increasingly been exploiting this process by filing baseless and redundant petitions in an effort to delay FDA approval of generic drugs. As one generic drug executive observed in Senate testimony:

> Frequently, a brand company will file a frivolous petition on the eve of FDA approval of a generic equivalent. This despite the fact that the FDA may have already granted a tentative approval, meaning that FDA already determined the generic product is safe and effective. The brand strategy is that it will take several months for the FDA to decide the petition, during which time approval of the generic drug is held in limbo. The brand is not required to submit petitions with merit. What the brand company can do is block competition for several months beyond the life of the 20-year patent, thereby extending its monopoly on the market.

Heather Bresch, Senior Vice President of Strategic Corporate Development for Mylan Laboratories, Testimony before the Senate Aging Committee, "Hearing on Generic Drugs," July 20, 2006.

25. In order to slow the approval process citizen petitions have often been submitted on the eve of the completion of the FDA review, which is when the pharmaceutical company's patent expires. These petitions are often based on information available well before the petitions are submitted. The citizen-petition approval process is time consuming, and despite tentative

approval of the generic drug it could take several months for the FDA to respond to a petition. The qualified generic is held in administrative limbo, and consumers suffer as lower-cost alternatives are kept off the market.

26. Recognizing the likelihood of abuse during the citizen-petition process, Congress amended the Federal Food, Drug, and Cosmetic Act in 2007 to expedite the process and improve transparency. FDA Amendments Act of 2007, 21 U.S.C. 355(q) (the "2007 Amendments"). Under the new law the FDA must take final action on a petition within 180 days of the petition's submission. This period cannot be extended for any reason, including review of supplemental information filed by the petitioner or comments filed by others. The Amendments provide that the FDA shall not delay approval of a pending ANDA because of a citizen petition unless the FDA determines that a delay is necessary to protect the public health. The 2007 Amendments also authorize the FDA to summarily deny any citizen petition whose primary purpose, as determined by the FDA, is to delay competition. Prior to this 2007 amendment, the FDA maintained a practice of considering and responding to relevant citizen petitions prior to approval of an ANDA to assure that the petitions did not present any new issues or issues of concern which may alter the approval of an ANDA.

27. Signed into law on September 27, 2007, these revisions were not yet in effect at the time the FDA was considering the petitions filed by Astellas at issue here.

28. During this pre-amendment period, the resulting delay of generic competition can be lucrative for a brand name manufacturer facing impending competition from an AB-rated generic. The cost of filing an improper, sham citizen petition was minor in comparison to the value of securing an additional period of monopoly profits. Under the FDA's regulations, the agency was to respond to citizen petitions within six months. In practice, it was common for the

FDA to take longer than six months to respond, especially if the citizen petition raised numerous technical issues that would require input from various disciplines.

29. Citizen petitions regarding the approvability of generic products rarely led to any change in the FDA's policy on the basis of data or information submitted in the petition. In 2006, Gary Buehler, Director of the FDA's Office of Generic Drugs ("OGD"), stated that:

> An analysis of petitions answered between calendar years 2001 and 2005, raising issues about the approvability of generic products (42 total responses), showed that FDA denied 33, denied three in part and granted six.
>
> … it is noteworthy that very few of these petitions on generic drug matters have presented data or analysis that significantly altered FDA's policies.

V. FACTUAL BACKGROUND

A. Organ Transplantation and Immunosuppresant Therapy

30. Although there are currently more than over 100,000 patients awaiting organ transplant, due to the scarcity of organs, only about 28,500 transplants were conducted in 2009.

31. Given the scarcity of organs, every effort is made to ensure that that the patient remains in good health and that the body does not reject the transplant. Organ rejection occurs when the body has an immune response to the transplanted organ, that is, the body's immune system recognizes the organ as foreign and attacks it, leading to transplant failure and removal of the transplant from the body.

32. Rejection can be minimized through matching the compatibility of the donor to the recipient based on various markers *(e.g.,* blood type and other factors) and through the use of drugs that suppress the immune system -- immunosuppressants.

Calcineurin Inhibitors

33. While there are various types of immunosuppressants used to treat transplant recipients, the two primary immunosuppressants prescribed to prevent organ rejection are cyclosporine and tacrolimus (Prograf), both of which are calcineurin B inhibitors. Calcineurin is an enzyme that activates "cytotoxic T-cells", a group of white blood cells that are part of the immune system. These T-cells attack foreign cells in the body, such as virally infected cells and tumor cells. Activated cytotoxic T-cells sometimes recognize the transplanted organ as foreign cells and attempt to destroy it causing a rejection of the transplanted organ. Calcinueurin inhibitors inhibit the T-cell activation via the calcineurin pathway, and thereby prevent the immune system response that leads to organ rejection.

B. Prograf

34. Astellas manufactures, markets, and sells Prograf (tacrolimus), a brand name prescription drug. Tacrolimus, the active ingredient, is an immunosuppressant indicated for the prevention (prophylaxis) of organ rejection in patients who have had liver, kidney and heart transplants. Tacrolimus is derived from a metabolite produced by the bacteria *Streptomyces tsukabaensis.*

35. The FDA approved the sale of 1 mg and 5 mg capsules of Prograf on April 8, 1994.[1] On August 24, 1998, the FDA approved the use of 0.5 mg capsules of Prograf.

36. Prograf is administered orally twice daily, in capsule form. The labeling includes a boxed warning for the healthcare professional that highlights special information or possible complications associated with the drug. The warning states that only physicians experienced with immunosuppressive therapy and management of organ transplant patients should prescribe

[1] On March 29, 2006, FDA granted an Orphan Drug Exclusivity for Prograf (capsules and injection) for the prevention of organ rejection post-heart transplantation. This exclusivity ends on March 29, 2013.

Prograf, that patients receiving Prograf should be carefully monitored in an appropriate medical setting, and that physicians should monitor and follow-up with patients taking Prograf.

37. Immediately post transplant, higher dosages of tacrolimus are administered; by six months post-transplant-the dosages are reduced.

38. Further monitoring of the tacrolimus blood concentration with other laboratory and clinical tests are essential for patient management to evaluate possible organ rejection, or drug toxicity, dose adjustments and patient compliance. Monitoring is required for as long as the patient is on immunosuppressant therapy, although the initial frequency is reduced to about once per month the longer the patient remains on therapy.

39. Prior to August 10, 2009, Prograf held 100% of the relevant market for tacrolimus capsules. According to IMS Health, a leading pharmaceutical market research firm, Astellas had annual sales of approximately $929 million for the twelve months ending April 2009.

40. As a sophisticated and long-standing pharmaceutical manufacturer Astellas knew that generic manufacturers would seek approval from the FDA to market a generic version of Prograf.

41. On December 28, 2006, Sandoz Inc. filed an ANDA to market and sell tacrolimus capsules in 0.5 mg, 1mg, and 5 mg dosages.

VI. Astella's Unlawful Attempt to Delay Generic Competition for Prograf

A. The FDA's Preparation for Approval of Generic Competition for Prograf

42. The goal of bioequivalence testing between a pioneer product and generic product is to determine whether there is a "lack of significant difference" in the rate and extent of absorption of the drug between the brand name and proposed generic. Federal statutes require that in evaluating generic drugs for approval, the FDA uses its own scientific judgment in

determining the methods used to uncover whether a lack significant of difference between the RLD and generic products exists and if the tests, methods, and data are sufficient to approve or deny the ANDA application. To advise the pharmaceutical industry and the public on what information the FDA considers appropriate to demonstrate bioequivalence, the FDA may publish documents called Guidance for Industry ("Guidance").

43. Guidances merely provide the industry and other interested parties of the FDA's latest thinking on certain topics. As the FDA website and each guidance specifically states, "Guidance documents represent the Agency's current thinking on a particular subject. They do not create or confer any rights for or on any person and do not operate to bind the FDA or, the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both." [2]

44. In October 2000, the FDA published Guidance for Industry, Bioavailability and Bioequivalence Studies for Orally Administered Drug Products-General Considerations ("General Bioequivalence Guidance"), which provided the FDA's then current view on *in vitro* and *in vivo* testing for establishing bioavailability and bioequivalence in NDAs and ANDAs for orally administered drug products.[3]

45. For bioequivalence determinations, FDA recommends single-dose bioequivalence studies conducted in healthy subjects, as opposed to multi-dose studies[4] or those conducted in transplant patients.

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[2] *See, e.g.*, U.S. FDA website, ;'Guidance~" page, at http://www.fda.gov/Drugs/GuidanceComplianceRegulatorylnforrnation/Guidances/default.htm

[3] The FDA published a revised version of this Guidance in March 2003.

[4] Multiple-dose or steady state bioequivalence studies "are generally conducted in patients" as opposed to healthy volunteers. Janet Woodcock, Director of FDA's Center for Drug Evaluation and Research, to William Fitzsimmons, Astellas Pharm USA Inc. Senior Vice President, re: Docket No. FDA-2007-P-OI I 1, dated August 10,2009 ("FDA Petition Response") at 7.

46. The FDA's recommendation is based on its belief that single dose studies in healthy subjects are more sensitive at detecting the differences in formulation and other product-related characteristics that may affect the bioequivalence of assessment. *See* FDA Petition Response at 7, n. 12 (citing El-Tahtawy, AA, *et al., Comparison of single and multiple dose pharmacokinetics using clinical bioequivalence data and Monte Carlo simulations*. Phar. Research. 11:1330(1994).

47. The reason that single-dose studies in healthy subjects are more sensitive than multiple-dose (steady-state) studies in sick patients for bioequivalence testing is that using sick patients introduces variability related to the disease state that might confound or impede the analysis of bioequivalence, without yielding any greater ability to detect differences in formulation that might have clinical significance and that would not be detected by bioequivalence studies in healthy subjects. Similarly, for systemically acting drugs (like tacrolimus), single-dose studies are typically more sensitive in assessing release of a drug substance from the drug product into systemic circulation. The 2000 General Bioequivalence guidance recommended that pharmacokinetic and pharmacodynamic studies designed to assess bioequivalence be conducted as single-dose studies in healthy adult subjects representative of the general population, taking into account age, sex, and race.

48. The FDA's recommendation for using single-dose studies in healthy subjects has been applied since 2000 and was the same bioequivalence criteria applied to brand name products when they undergo formulation changes. Like generic drugs, these reformulated brand name products are generally not tested in a clinical population. Furthermore, this bioequivalence testing criteria has been applied by the FDA not only in approving generic versions and/or branded product changes for drugs that are used in relatively healthy patients,

but also for approving generic version and changes in branded versions of Narrow Therapeutic Index ("NTI") or Critical Dose ("CD") drugs, such as immunosuppressants used in transplant patients.

49. One example where generic versions of a critical-dose, NTI immunosuppressant drug used in transplant patients were approved based on the single-dose, healthy-patient-bioequivalence tests is the approval of generic versions of cyclosporine since at least 2002. The importance of the fact that the single-dose, healthy-patient bioequivalence standard worked correctly regarding cyclosporine generics is that during the past decade, the FDA has not become aware of any safety signals regarding brand to generic substitution for cyclosporine drug products. Moreover, none of the generic cyclosporine products that properly implemented the FDA-recommended bioequivalent studies in healthy patients have been removed from the market due to safety concerns.

B. The 2007 Guidance for Bioequivalence Testing Standard for Tacrolimus

50. In May 2007, the FDA published a *Guidance for Industry, Bioequivalence Recommendations for Specific Products* for tacrolimus ("the Tacrolimus Guidance"). Under the Tacrolimus Guidance, sponsors were directed to measure tacrolimus in whole blood, with bioequivalence of tacrolimus using the standard bioequivalence criteria of 80- 125% for both peak blood concentration (Cmax) and the area under the plasma-time concentration curve (AUC) at the 90% confidence interval. Studies in the 0.1 mg and 1.0 mg dosages were not necessary if acceptable bioequivalence was shown with the 5.0 mg strength and where proportional similarity across the strengths was shown and the sponsor provided acceptable dissolution tests of all strengths.

51. Consistent with its prior position on bioequivalence, the FDA's Tacrolimus Guidance recommended that sponsors demonstrate bioequivalence of generic tacrolimus through two studies involving single-dose studies in healthy volunteers. The difference being one study was to be conducted in a group fasting, while the other would be in a fed group. The Guidance did not require a multiple-dose bioequivalence studies in a transplant patient population.

C. Astellas' Unlawful Attempt to Delay Generic Competition for Prograf

52. On September 21, 2007, Astellas filed a citizen petition with the FDA seeking to delay the FDA approval of generic tacrolimus capsules. Astellas Citizen Petition ("Petition"), dated September 21, 2007, was filed a week before the new law became effective that prohibited the use of abusive citizen petitions. Astellas stated that the petition was filed in response to the FDA's publication of the Tacrolimus Guidance. On September 11, 2008, Astellas filed a supplement to the citizen petition.

53. Astellas' citizen petition did not address the adequacy of Sandoz's ANDA, nor did it present any evidence that Sandoz's tacrolimus failed to demonstrate bioequivalence to Prograf, or raise any valid concerns about public health.

54. Astellas' Petition argued that single-dose bioequivalence studies in healthy patients were insufficient to establish bioequivalence between branded and generic tacrolimus, and that ANDA applicants should be required to conduct multiple-dose bioequivalence studies in transplant patients. Although Astellas bore the burden, as petitioner, to provide evidence to FDA to support its challenge to FDA's recommendation that bioequivalence testing for generic tacrolimus could be done through single-dose studies on healthy patients, Astellas did not raise any scientific evidence that the single-dose studies were insufficient to assess bioequivalence between the two products. In fact, Astellas' Petition failed to disclose that Astellas had

repeatedly and consistently represented to various regulatory agencies that single-dose studies were appropriate for testing bioequivalence for tacrolimus.

55. The Petition ended with the certification required under 21 C.F.R. § 10.30: "The undersigned certifies to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, *and that it includes representative data and information known to the petitioner that are unfavorable to the petition.*" (emphasis added). The Petition was signed by William E. Fitzsimmons, Pharm.D., M.S., Senior Vice President; Research and Development, Astellas Pharma US, Inc. Astellas' Petition did not include all unfavorable information known to Astellas.

56. Astellas' citizen petition requested that the FDA:

- require ANDA applicants for immunosuppressant drugs such as tacrolimus demonstrate bioequivalence to innovator products in transplant patients, in addition to healthy subjects, in direct contradiction to the FDA's longstanding practice of requiring the demonstration of bioequivalence only in healthy subjects in order to reduce the introduction of confounding variables (like disease state) on bioequivalence studies;

- require labeling changes for all orally administered immunosuppressant drugs used in transplant patients that are characterized as having a narrow therapeutic index, which Astellas argued included tacrolimus, to add warnings and precautions regarding the substitution of generics for the innovator product, even though AB-rated generic products are bioequivalent to the innovator product and it has long been the FDA's practice to treat such products as interchangeable;

- add a section to the Orange Book that highlights risks associated with switching patients among different oral formulations of immunosuppressants, such as tacrolimus despite the FDA's practice, and many states' requirements, of complete interchangeability of innovator and AB-rated generic products; and

- require generic manufacturers to distinguish their product from branded products by use of different color capsules or container closure.

D. The Petition Lacked any Objective Basis in Scientific Evidence.

57. Based on its prior assertion in regulatory filings that single-dose studies with healthy patients are sufficient to establish bioequivalence between its own tacrolimus products, the Petition did not proffer any scientific evidence that such studies were not a sufficient means for bioequivalence testing. Astellas did not dispute the FDA's position that single-dose studies, like the ones called for in the bioequivalence guidelines at issue, are more sensitive than multi-dose, in-patient studies are predicting differences resulting from differences in formulation. Rather, the Petition raised arguments based on three categories of information, which the district court subsequently described as "entirely speculative." In fact, several scientific studies that Astellas cited in its petition contradicted Astellas' position by providing scientific evidence that the single-dose healthy-patient bioequivalence studies recommended by the FDA were accurate indicators of bioequivalence between generic and brand immunosuppressants.

58. *First*, Astellas recounted the approval of branded and generic cyclosporine and the withdrawal of generic cyclosporine, which had been approved based on single-dose, healthy-patient bioequivalence studies to call into question potential problems with the FDA's recommended bioequivalence protocol.

59. Astellas' Petition cited studies comparing branded and generic cyclosporine in transplant patients, arguing that they suggested that bioequivalence in healthy volunteers does "not necessarily translate to clinical equivalence when comparing both generic and branded [immunosuppressants] in transplant patients." *Id.* These included:

- Roza and colleagues (2002) compared fifty kidney transplant patients on Neoral, who were converted to generic cyclosporine on a dose per dose basis, then two weeks later converted back to Neoral. According to Astellas, "no dosing adjustments were required following conversion between formulations of cyclosporine" and there were no differences in the pharmacokinetic parameters, (C_{max}, AUC, T_{max} and C_{min}). Astellas concluded that although the "study was not powered to show statistical differences between

subpopulations," the authors found no differences in pharmacokinetics of cyclosporine based on gender, race, or presence of diabetes with either the generic or branded cyclosporine.

- Carnahan and colleagues (2003) also reported a study comparing the conversion of forty-one kidney transplant patients from branded to generic cyclosporine. The authors found no significant differences observed in patients whose blood levels showed therapeutic levels of cyclosporine. No changes in dose were required when the patient was converted to the generic form.

- Fradette and colleagues (2005) evaluated the pharmacokinetics of conversion between branded and generic cyclosporine in thirty-seven stable kidney transplant patients. Patients were converted to generic cyclosporine on a dose per dose basis, and after two weeks of treatment, were converted to the brand product. "On average, C_{max} and AUC observed after administration of branded or generic, cyclosporine were not statistically different." Some intra-patient variability was observed after treatment with the generic product when compared to the branded product; however this variability was not significantly significant.

- Taber and colleagues (2005) reported on 188 kidney transplant patients treated with either branded (n=1 00) or generic (n=88) cyclosporine. Patients on the 19 branded product were studied from January 1999 to May 2001; patients on generic product were studied between May 2001 and July 2002. Patients received the same initial dose of cyclosporine and were targeted to have the same "trough levels" in the blood. Adjunctive agents (corticosteroids and mycophenolate mofetil) were allowed in both groups. Six months post transplant, patients receiving generic cyclosporine had statistically significant higher proportion of acute rejection (39% v.25%). –

- Qazi and coworkers (2006) revaluated 82 kidney transplant patients who were converted from branded to generic cyclosporine on a dose for dose basis. Seventy-three patients switched to the generic, while nine remained on the brand cyclosporine and served as a control group. The authors reported that 18% of the patients on the generic cyclosporine required dose adjustments, whereas none of the control group did.

Id. at 7-10.

60. Although Astellas acknowledged that three of the five studies showed no difference between branded and generic cyclosporine, its Petition still asserted that studies in healthy volunteers are inconclusive at best to establish bioequivalence for use in transplant

patients. Petition at 10. Given the literature on the subject, Astellas argued that, "questions arise as to whether the current standard for bioequivalence is sufficient to support indiscriminate substitution of alternate formulations of immunosuppressants in vulnerable transplant patients." *Id.* at 7.

61. Astellas, however, failed to disclose significant limitations in those studies due to which no meaningful conclusions could be reached regarding whether generic cyclosporine was (or was not) bioequivalent to brand cyclosporine. For example, a 2005 study by DJ Taber and colleagues compared the transplant rejection levels among 188 kidney transplant patients treated from January 1999 to May 2001 with branded cyclosporine versus the rejection levels of 88 patients treated from May 2001 to July 2002 with generic cyclosporine, Astellas asserted that the study found that the patients treated with generic cyclosporine had a much higher level of organ rejection which was “clinically significant.” However, as the FDA noted in rejecting Astellas’s petition, Astellas failed to acknowledge important limitations of conclusions, which the author acknowledged in his study – *i.e.* that the studies compared patients who were treated at different times and differences in dosing changes or adjustments were not taken into account. Thus, Astellas lacked any scientifically valid or statistically justifiable basis for asserting that the results of the study reflected differences in the generic and branded formulations. Similar, regarding a 2006 study by YA Qazi and colleagues, Astellas failed to acknowledge other study limitations which rendered any conclusions regarding brand-generic bioequivalence meaningless.

62. For further support for its requests for additional testing in transplant patients, Astellas cited to reports from the National Kidney Foundation (1999) recommending that, tacrolimus be designated on the "critical drug category," mandating further studies in transplant

populations and subpopulations for demonstrating bioequivalence, and recommending patient and physician education regarding the risks associated with switching to a generic immunosuppressant. Petition at 10. According to Astellas, the American Society of Transplantation ("ASTS") published similar recommendations in 2003; however, the experts acknowledged that with proper patient follow-up and monitoring, generic immunosuppressants, including those with NTI, appeared to provide adequate immunosuppression. *Id.* at 10-11.

63. The petition then argued that "limited clinical data"and the recommendations of the two organizations demonstrated that bioequivalence established in healthy volunteers could result in significant risks to transplant patients who are "indiscriminate[ly]" switched to generics " without notice to the patient or physician. *See id.* According to Astellas, high intrapatient (same patient) variability in transplant patients also mandated the conclusion that bioequivalence studies in healthy volunteers may not sufficiently predict blood levels in individual patients. *Id.* at 12. Again citing to the Taber study, Astellas argued that bioequivalence of gen*eric to* branded cyclosporine in a population of healthy volunteers did not correlate to bioequivalence within an individual patient. *Id.* at 12.

64. Astellas concluded that not only does bioequivalence in healthy patients not adequately correlate to bioequivalence in transplant patients as a whole, it does not translate to interchangeability in the individual patient. *Id.* The remedy suggested by Astellas was to add bioequivalence studies in transplant patients for bioequivalence determinations. *Id* at 14.

65. Astellas also cited several journal articles that described factors that impact the ability to maintain adequate blood levels of tacrolimus. *Id*. at 14-18. These factors included patient disease state, time since transplant, concurrent medications, organ transplanted, race, age, and whether the drug was taken in a fasted or fed state, and with the particular meal (high

fat, low carbohydrate). Since differences may exist between generic and branded products, Astellas requested that these factors be considered in designing bioequivalence studies in patients. *Id.* at 18. "[T]aking into account the limitations of current bioequivalence standards in assessing the impact of switches at the individual level, along with interpatient factors discussed above, the performance of studies healthy volunteers is inadequate to insure patient safety." *ld.*

66. The petition then discussed Astellas' difficulties in demonstrating bioequivalence for an extended release form of tacrolimus called Advagraf that would provide the same total daily dose as the immediate release Prograf. According to Astellas, despite meeting the FDA's bioequivalence requirements in healthy volunteers, significant differences were observed in *de novo* kidney and liver transplant patients: extended release tacrolimus showed significantly reduced blood levels on day one. Thus, bioequivalence in healthy volunteers did not predict the pharmacokinetics of the drug in transplant patients early after surgery. *ld.* at l8-19. The FDA bioequivalence studies should require the monitoring of pharmacokinetics immediately after the transplant to ensure that adequate blood levels are maintained according to Astellas. *ld.*

67. Astellas then requested that patients and physicians be notified of any substitution of branded tacrolimus for generic tacrolimus as a way to mitigate potential risks to the patient on the theory that notification would ensure that physicians would increase the monitoring of patients who were switched to a generic tacrolimus.

68. Astellas' final request asked the FDA to require manufacturers of generic versions of NTI drugs, such as tacrolimus, to differentiate their products from Prograf by color/shape of capsule, container closure, packaging, and source so that patients and pharmacists would be aware of a change in source of the drug. *Id.* at 21. Such a differentiation would reduce the potential for medication errors according to Astellas. *Id.*

69. Astellas filed a supplement on September 11, 2008, requesting that the FDA consider comments from the ASTS that had been submitted to the FDA during development of a draft guidance document for tacrolimus.

E. The FDA Sees Astellas' Citizen Petition for What lt Is: A Blatant Attempt Slow the Process of Approval of Generic Competitors

70. On August 10, 2009, nearly two years after Astellas filed its Petition, the FDA responded in a detailed fifteen page letter, which denied Astellas' request. Janet Woodcock, Director of FDA's Center for Drug Evaluation and Research, to William Fitzsimmons, Astellas Phann USA Inc. Senior Vice President, re: Docket No. FDA-2007-P-0111, dated August 10, 2009 ("FDA Petition Response"). On the same day, the FDA also approved Sandoz's ANDA for generic tacrolimus capsules, filed nearly three years earlier.

71. The FDA petition response reiterated its position, consistent with the General Bioequivalence Guidance and the Tacrolimus Guidance, that ANDA applicants need not conduct additional clinical trials for bioequivalence in transplant patients. The goal of bioequivalence is to determine if significant differences exist in the rate and extent of absorption between innovator and generic formulations. When bioequivalence is proven, the generic product can be substituted for the innovator product and can be expected to have the same safety profile and clinical effect as the innovator product. *ld.* at 6-7. The FDA stated that "with regard to tacrolimus, there is insufficient scientific evidence to suggest that the use of specific patient population(s) in bioequivalence studies would detect differences in formulation that might have clinical significance and that would not be detected by bioequivalence studies in healthy subjects. *Id*. at 6-7.

72. The FDA systematically dismantled the arguments advanced by Astellas concerning the cyclosporine studies and finding that "the literature cited in your petition does

not provide sufficient evidence to show that the current the FDA standards for generic approval of immunosuppressants such as tacrolimus, fail to support substitution of alternate formulations of these drugs in transplant patients." *Id.* at 9. For example,

- Roza did provide information on the bioequivalence of a generic cyclosporine with the innovator product in stable renal transplant patients. The findings in Roza actually suggest that a bioequivalence in healthy volunteers can be predictive of bioequivalence in stable renal patients. FDA Petition Response at 9.

- The Canahan study did not provide any meaningful conclusion on the interchangeability of generic cyclosporine with the innovator product. *Id.*

- Fradette's data was consistent with the Roza data, showing that bioequivalence in healthy subjects was predictive of bioequivalence in renal transplant patients. Further, the FDA stated, the conclusions Astella reached on greater intrasubject variability were not supported by the data in Fradette. *Id.8-9.*

- • For Taber, the FDA replied that Astellas failed to cite the important limitations of the conclusions as acknowledged by Taber: that the studies compared were performed at different times, and the limits on analyzing the intrapatient variation because of the dosing strategies, not the formulation. *Id.*

- • The Qazi study did not provide enough information on patient randomization, sample size of treatment groups, or data analysis to provide any meaningful conclusions regarding safety and efficacy of the generic product and innovator product. *Id.* at 9.

73. The FDA also took issue with Astellas' comparison of Advagraf to Prograf pharmacokinetic data generated in healthy volunteers and stable kidney and liver transplant patients, which Astellas argued did not predict bioequivalence in *de novo,* kidney or liver transplant patients in the immediate postoperative period. "Your example includes two different types of products: an immediate release product and an extended release product. These products are not pharmaceutically equivalent to each other... [F]or the purpose of generic approval, the two would not be considered therapeutically equivalent even if the 90% confidence interval....for AUC and C_{max} fall within the 80-125% limits." FDA Response at 11. Astellas' comparison was not applicable to the approval of generic tacrolimus. *Id.*

74. The FDA also rejected Astellas' request to conduct bioequivalence studies in organ specific transplant patients. The FDA responded that patient related factors on the pharmacokinetic measures of tacrolimus are related to the active ingredient. "Since a generic product will contain identical amounts of the same active ingredient in the same dosage form as the [innovator product], the impact of patient related factors on drug exposure is not expected to differ between the [generic] 25 and [innovator] products." *Id.* at 11. Furthermore, bioequivalence studies in transplant patients are subject to additional sources of variation which would impede the analysis of finding formulation differences. *Id.* Finally, the FDA stated that ASTS failed to supply scientific or clinical data to support the need for bioequivalence studies in organ-specific transplant patients. *Id.* at 12. As to additional warnings, the FDA denied these requests, stating that if the generic drug is found to be bioequivalent, it is interchangeable with the branded counterpart and additional warnings are not needed: the "ANDA review process [is] sufficient to ensure that the generic versions of immunosuppressant drugs are equivalent with respect to their safety and efficacy for use under conditions suggested in their labeling." FDA Petition Response at 14.

75. Finally, the FDA denied Astellas' request to require differentiation between branded and generic tacrolimus by shape, color, or some other method of distinguishing. A generic product may have a different shape or color from the innovator, it i*s no*t required to do so. A generic product is expected to be substitutable for its branded product such that it will produce the same clinical effect and safety profile as the branded product.

76. The FDA concurred with Astellas that differing dosages of strengths of generic tacrolimus be distinguishable from one another. *Id.* at 14-15. The FDA has always required

differentiation among dosages, and thus this request did not change or alter any FDA practice or treatment of the ANDA.

77. Finally, the FDA noted that Astellas ' supplement merely reiterated concerns expressed in its petition and did not provide any additional scientific data to support its position.

78. On August 10, 2009, the FDA denied Astellas' citizen petition requests and approved Sandoz's ANDA.

F. Astellas' Baseless Application for a Temporary Restraining Order and Preliminary Injunction

79. On August 11, 2009, in a desperate attempt to delay generic entry to the market, Astellas filed a motion for a temporary restraining order ("TRO") and a preliminary injunction in the District of Columbia, seeking to stay the FDA approval of generic tacrolimus capsules. Sandoz's generic capsules came to market the same day.

80. Astellas' application for TRO and preliminary injunction were objectively baseless in light of the extensive jurisprudence regarding the deference courts give to the FDA's scientific judgment. *See, e.g., Schering Corp. v. FDA*, 51 F.3d 390 (3d Cir. 1995); *Glaxo Group v. Leavitt*, AMD 06-469 (D. Md., Mar. 6, 2006) (Davis, J.); *Schering Corp. Sullivan*, 782 F. Supp. 645 (D.C. Cir. 1993); *Somerset Pharms, Inc. v. Shalala*, 973 F. Supp. 2d 443 (D. De. 1997); *Bristol-Myers Squibb Co. v. Shalala*, 923 F. Supp. 212 (D.D.C. 1996); *Fisons Corp. v. Shalala*, 860 F. Supp. 859 (D.D.C. 1994).

81. Astellas' filings with the court raised the same issues that were rejected by the FDA in the citizen petition and further argued that the FDA was acting in an arbitrary and capricious manner in denying its petition. Astellas argued that its evidence was "compelling" in showing the need for bioequivalence testing in transplant patients and that the FDA's response was "inadequate to the point of being arbitrary and capricious." Application of Plaintiff Astellas

Pharma US, Inc. for a Temporary Restraining Order and a Preliminary Injunction, USDC D.C. Case 1:09-cv-01511, docket no. 3; dated August 10, 2009 ("Astellas TRO Motion") at 22-23. Astellas also argued that the FDA's failure to warn of generic substitution was arbitrary and capricious and denied the safety and efficacy issues that Astellas raised. *Id.* at 25.

82. In an attempt to satisfy the requirements of a TRO, Astellas argued that it would suffer irreparable harm in the form of lost sales, price erosion, loss of goodwill and harm to its reputation. The balance of harms, Astellas argued, favored Astellas. The FDA would suffer no harm; a delay would also not harm its competitor Sandoz. Astellas implied that allowing Sandoz generic tacrolimus to come to market would destroy Astellas' business. *Id.* at 30.

83. Astellas argued that injunctive relief served the public interest because (i) it would require the FDA to comply with the law and (ii) the public has an interest in safe and effective generic products.

84. The FDA opposed the motion on August 12, 2009; the same day, and without oral argument, the court denied the TRO.

85. In its opposition, the FDA stated that its process for approving generic tacrolimus used the appropriate methods and standards, and was based on a thorough and rigorous review of relevant scientific evidence. Defendants' Memorandum in Opposition to Plaintiffs Motion for a Temporary Restraining Order and a Preliminary Injunction, USDC D.C. Case 1:09-cv-01511, docket no. 6, dated August 12, 2009 ("FDA Opposition") at 2.

86. Furthermore, the FDA pointed out that Astellas' citizen petition delayed the approval of Sandoz's generic: "Sandoz' [ANDA] was pending for over [2½] years. At least part of this period was directly attributable to the need to evaluate and respond" to Astellas' citizen petitions. Astellas' citizen petition arguments were "*yet another instance in which a*

manufacturer of a pioneer drug product in fear of losing its lucrative monopoly has attempted to block generic competition by challenging the scientific basis for the FDA's approval of a generic." *Id.* (emphasis added).

87. On August 17, 2009, the Court issued its opinion describing its reasoning for denying the TRO. In denying Astellas' request for a TRO, the Court stated that "FDA produced a comprehensive response to [Astellas'] Citizen Petition and provide a detailed justification for its conclusion[s]." Memorandum Opinion Denying the Plaintiff's Motion for a Temporary Restraining Order and Preliminary Injunction, USDC D.C. Case 1:09-cv-01511, document no. 10, dated August 17, 2009 ("Opinion") at 13.

88. On August 17, 2009, the Court issued its opinion describing its reasoning for denying the TRO and Preliminary Injunction. In denying Astellas' request for a TRO and preliminary injunction, the Court stated that "FDA produced a comprehensive response to [Astellas'] citizen petition and provided a detailed justification for its conclusion[s]." Memorandum Opinion Denying the Plaintiff s Motion for a Temporary Restraining Order and Preliminary Injunction, USDCD.C. Case ·1:09cv- 01511, docket no. 10, dated August 17, 2009 ("Opinion") at 13.

89. On August 19, 2009, Sandoz moved to intervene in the case; the Court granted this motion on August 21, 2009. On November 24, 2009, Astellas voluntarily dismissed the case.

G. Astellas' Anticompetitive Conduct

90. Astellas' Petition and subsequent litigation were a sham. Astellas could not reasonably have expected to prevail on the substance of the petition or the lawsuit.

91. The arguments advanced in Astellas' Petitions were objectively baseless from regulatory and scientific perspectives. Astellas was aware that its arguments would fail at the

FDA. The Petition was filed with the intent to delay the FDA approval of generic tacrolimus capsules. According to the FDA, the Petition successfully delayed the approval of generic tacrolimus capsules by nearly two years.

92. Astellas made arguments in the citizen petition that have been repeatedly rejected when the other innovator citizen petitions sought to prevent generic approval. The arguments were knowingly frivolous.

93. The statutory and regulatory basis for bioequivalence are clear: if the generic product has the same dose, strength, and route of administration, form and blood plasma levels as innovator product, the generic is fully substitutable for the branded product. 21 U.S.C. §355(j)(2)(A). The generic product is relying on the findings of safety and efficacy of the branded drug. Thus with tacrolimus, any safety and efficacy issues with the branded product, including dose management issues in transplant patients, would apply to the generic product as well. As the FDA said, as long as the generic has the same dosage; strength and route of administration as the branded product, the issues with inter-patient variability apply equally to both innovator and generic product. This is consistent with the law and the regulations, and the FDA has repeated these statements in many citizen petition responses and in draft guidance documents, including the guidance documents for oral dosage forms for tacrolimus.

94. Astellas' own briefing demonstrates that their argument were objectively baseless. Astellas cites to the studies of cyclosporine for support for the need for bioequivalence studies in transplant patients. However, as the FDA stated, the cyclosporine studies failed to support Astellas' assertion outright or were inconclusive because of study design. The FDA noted that some of the studies of bioequivalence for cyclosporine generics were conducted on healthy patients and were in fact predictive of bioequivalence in transplant patients.

95. Astellas clearly was aware of the information in these studies as it selectively picked the information from them to present to the FDA in support of its arguments. Astellas cited to cyclosporine bioequivalence articles that were either inconclusive or demonstrated that bioequivalence assessments in healthy volunteers were transferrable to transplant patients, positions which are contrary to its arguments. Furthermore, Astellas failed to include in its argument that the authors in the Taber study acknowledged the limitations of their conclusions.

96. Astellas' arguments in support of its Petition were based on misrepresentations and omissions such that no sophisticated pharmaceutical company in its position could expect to prevail. For this reason, Astellas' arguments constitute fraud on the FDA and the FDA relied on the arguments in making a diligent and time-consuming investigation into their validity.

97. The misrepresented conclusions and omissions of key information from these studies in support of its own arguments render false the certification signed by Astellas acknowledging its duty to supply information contrary to its position to the FDA.

98. Astellas' argument that drugs such as tacrolimus and cyclosporine have special problems requiring additional bioequivalence studies in transplant patients belies the fact that the FDA has experience in assessing bioequivalence in this class of drugs. The FDA has also published guidance documents for the industry on assessing bioequivalence in calcineurin B inhibitors.

99. Astellas' argument that neither healthy volunteers nor a single-dose study were sufficient for bioequivalence studies is contradicted by its own package insert. Astellas used healthy volunteers to assess bioequivalence between the 1 mg and 5 mg capsules: "A single dose study conducted in 32 healthy volunteers established the bioequivalence of the 1mg and 5

mg capsules. Another single dose study in 32 healthy volunteers established the bioequivalence of the 0.5 mg and 1 mg capsules."

100. The request for labeling changes to alert clinicians and patients of switching between generic and branded product is also baseless. Because by law an AB rated approved generic product is the same as the branded product, the labeling requirements of the branded product apply to the generic. In this particular class of drugs, doctors are routinely monitoring patients for changes and would detect any problems, whether related to dose, source, rejection, or disease state. For example, the prescribing information highlights, in a prominent black box warning, the requirement for routine monitoring of blood concentration, renal and liver function testing, and tissue biopsies.

101. The additional request that the sources of product be identified by color or container closure is also baseless. AB rated generics are supposed to be completely interchangeable from branded reference products. The FDA did agree with Astellas that the different strengths should be clearly identified - the FDA routinely requires different dosage forms of the same drug to be distinguishable.

102. Astellas knew that the FDA and the courts would not find in its favor. Astellas, as a sophisticated pharmaceutical company, is aware of the long line of cases that provide deference to the FDA's scientific determinations. Additionally, such a sophisticated pharmaceutical company would have been aware that courts were routinely finding for the FDA in court challenges over its citizen petition denials. [5]

[5] *FDA Racks Up Another Winning Bioequivalence Litigation; This Time Over Generic EFUDEX*, FDA Law Blog, Oct. 19, 2009 ("The district court's decision leaves intact FDA's stellar batting average in bioequivalence decision court challenges. Courts have uniformly held that FDA's bioequivalence determinations fall squarely with in the broad discretion of the Agency.") available at http://www.fdalawblog.net/fda_law_blog_hyman-'phelps/2009/l O/fda-racks-up-another-win-in-bioequivalencelitigation- this-time-over-generic-efudex.html

103. Not surprisingly, the FDA found Astrellas' TRO request to be wholly without merit: "Astellas has not articulated sound public policy grounds for supporting its arguments;" "[a]n assumption underlying Astellas' argument is that the Agency's approval standards will, upon further examination, be found inadequate. This assumption is too speculative and too unlikely to form the basis of a public policy argument for grant of a stay." *Id.* at 20. The FDA further stated that "One of the purposes of the Hatch-Waxman Amendments is to foster the availability of low-cost generic drugs. This important public policy would be frustrated if the FDA were to grant the stay Astellas' requests." *Id* at 24.

104. The FDA explicitly criticized Astellas' attempt to monopolize the market and reprimanded the company, stating: "[t]he policies behind Hatch-Waxman dictate that Astellas should not be permitted to shield its market share when the Agency has reasonably determined that competing generic drug products may be approved under section 505(j) of the Act." *Id.*

105. Further underscoring that the purpose of the citizen petition was solely to delay competition, Astellas filed the citizen petition only a few days before the new law that eliminated just this type of abuse of the citizen petition process became effective. *See supra* para. 27.

VII. ASTELLAS' ANTICOMPETITIVE ACTIONS HARMED THE PLAINTIFF AND CLASS MEMBERS

106. Although the FDA denied Astellas' Petitions in a fifteen-page letter, finding the Petitions to be without merit, Astellas' submissions had their desired effect and unlawfully extended the company's monopoly in the United States, by almost two years.

107. Astellas did not make its Petition with the FDA to influence FDA policy or address any legitimate concern about the efficacy or safety of generic tacrolimus. Rather, Astellas intended to forestall generic competition in the United States market for tacrolimus

during the time it would take the FDA to evaluate and respond its Petition. Astellas, with full knowledge that the FDA was very likely in the process of considering the bioequivalency of one or more generic products, waited until nearly the last possible moment before the law on citizen petitions changed to curb this type of abuse to submit its Petition to the FDA, hoping to impose significant delay into the consideration by the FDA of any generic competition. Although it argued that the Petition was in response to the Tacrolimus Guidance, this guidance had been published four months earlier and was publically available fourteen months earlier.

108. Given the FDA's limited resources and practice at that time of carefully considering all citizen petitions before granting final approval to ANDAs, Astellas knew that the filing of a citizen petition would immediately derail the FDA process for approving generic versions of Prograf. Astellas made its submissions to the FDA not to influence the FDA policy or procedure but instead to delay the FDA approval of generic Prograf and unlawfully extend the company's monopoly for Prograf products in the United States.

109. Astellas unlawful conduct denied Plaintiffs and the Class the benefits of free and unrestrained competition in the market for tacrolimus from September 21, 2007, (the date of Astellas' Petition) until August 10, 2009, (the date the FDA approved generic tacrolimus for sale in the United States). Further, the effects of Astellas' anticompetitive scheme extended beyond August 10, 2009 as the full extent and benefit of generic penetration does not occur immediately upon generic market entry.

110. Astellas 'unlawful actions denied Plaintiff and members of the Class the opportunity to purchase lower-priced AB-rated generic versions of Prograf and thus forced Plaintiff and members of the Class to pay supra-competitive prices for tacrolimus.

111. Astellas' actions are part of, and in furtherance of, the illegal monopolization scheme alleged herein, and were authorized, ordered, or done by Astellas' officers, agents, employees, or representatives while actively engaged in the management of Astellas' affairs.

VIII. RELEVANT MARKET

112. The relevant market is all tacrolimus capsule products - *i.e.*, Prograf (in all its dosage strengths and AB-rated bioequivalent tacrolimus capsule products).

113. The relevant geographic market is the United States.

114. Prior to generic entry in August 2009, Astellas held 100% market share in the relevant market. Following market entry by generic manufacturers and much cheaper generic version of Prograf, Astellas' market share for tacrolimus products declined dramatically in short period of time.

IX. MARKET EFFECTS

115. Astellas' acts and practices, as herein alleged, had the purpose and effect of unreasonably restraining and injuring competition by protecting Prograf from generic competition in the relevant market.

116. Had generic competitors been able to enter the relevant market and compete with Astellas, Plaintiff and the Class would have paid less for generics versions of tacrolimus instead of the higher priced Prograf. Regulations generally permit - and sometimes even mandate - pharmacists to substitute generic drugs for their branded counterparts, unless the prescribing physician has directed that the branded product be dispensed as written. Similarly, many third-party payors of prescription drugs *(e.g.*, PBMs and managed care plans) encourage or insist on the use of generic drugs whenever possible, thus creating a ready market for generic products.

117. The initial entry of generic products generally leads to a significant market share loss of a branded drug's sales within the first year as generic drugs can quickly and efficiently

enter the marketplace at substantial discounts. Astellas itself recognizes the effects of market entry of generic versions of a drug - both generally and in the specific instance of Prograf competition: affidavits submitted by Astellas in support of its application for a TRO stated that the company expected to lose a significant amount of the $74 million per month in North American sales. Astellas TRO Motion at 9 (citing to Declaration of P. Shea).

118. By preventing generic competitors from entering the market, Astellas injured Plaintiff and the other members of the Class in their business or property by causing them to pay more for tacrolimus products than they otherwise would have paid, Astellas' unlawful conduct deprived Plaintiff and other direct purchasers of tacrolimus products of the benefits of competition that Congress designed federal antitrust laws to preserve.

X. CLASS ACTION ALLEGATIONS

119. Plaintiff brings this action on behalf of itself and as a class action under Rule 23(a) and (b)(3) of the Federal Rules of Civil Procedure on behalf of the following class (the “Class”):

> All persons or entities in the United States and its territories who purchased Prograf (tacrolimus capsules) directly from Astellas (or any of its predecessors or affiliates) at any time from September 21, 2007 until the anticompetitive effects of Defendant's conduct ceased or ceases (the "Class"). Excluded from the Class are Astellas and its predecessors, officers, directors, management, employees, subsidiaries, parent or affiliates, and all governmental entities.

120. Plaintiff does not know the exact size of the Class at the present time. However, Plaintiff believes that due to the nature of the trade and commerce involved, there are over a hundred members of the class geographically dispersed throughout the United States such that joinder is impracticable. These direct purchasers may be identified from information and records maintained by Defendant.

121. Plaintiff's claims are typical of those of the Class and all members of the Classes are similarly affected by Defendant's wrongful conduct in violation of federal antitrust laws. All members of the Class were deprived of the benefits of competitive pricing for tacrolimus and of a competitive market for this product as a result of Defendants' unlawful conduct.

122. Plaintiff, as a representative of all Class members, will fairly and adequately protect the interests of all Class members. Plaintiff has engaged counsel who are highly experienced and competent in class action litigation and complex antitrust and consumer protection litigation. Plaintiff's interest is consistent with, and not antagonistic to, those of members of all Classes. An effective and practicable manner of notice to such members of all Classes can be fashioned by the Court.

123. Common questions of law and fact exist as to all Class members and predominate over any questions solely affecting individual Class members. Such common questions of law and fact include:

a. whether Astellas delayed or prevented generic manufacturers from coming to market in the United States;

b. whether the petitioning to the FDA by the Astellas was objectively baseless;

c. whether Astellas maintained its monopoly power by improperly delaying generic entry through, *inter alia*, the filing of sham citizen petitions with the FDA;

d. whether direct proof of Astellas' monopoly power is available, and if available, whether it is sufficient to prove Astellas' monopoly power without the need to also define a relevant market;

e. to the extent a relevant market or markets must be defined, what that definition is;

f. whether the activities of Astellas as alleged herein have substantially affected interstate commerce;

g. whether, and to what extent, Astellas' conduct caused antitrust injury to the business or property of Plaintiff and the members of the Class, and if so, the appropriate measure of damages; and

h. whether Plaintiff and all Class members are entitled to injunctive relief.

124. Prosecution of separate actions by individual Class members would create the risk of inconsistent or varying adjudications with respect to individual Class members that would establish incompatible standards of conduct for Defendant.

125. This Class action is superior to any alternatives for the fair and efficient adjudication of this controversy because:

a. It will avoid a multiplicity of suits and consequent burden on the courts and Defendant;

b. It would be virtually impossible for all Class members to intervene as parties-plaintiff in this action;

c. It is appropriate for treatment on a fluid recovery basis, which will obviate any manageability problems; and

d. It will provide court oversight of a claims process for all Class members, once Defendant’s liability is adjudicated.

126. Defendant has acted on grounds generally applicable to all Class members in that Defendant’s anticompetitive actions foreclosed competition in the market in which all Class members purchased tacrolimus. Accordingly, injunctive relief is necessary to protect all Class members from further antitrust injury.

127. Plaintiff knows of no difficulty that would prevent this case from being maintained as a class action. Class action treatment is a superior method for the fair and efficient adjudication of this controversy. Class action treatment will, among other things, allow a large number of similarly situated persons to prosecute their common claims in a single forum, thus avoiding the unnecessary duplication of resources that numerous individual actions would

require. Moreover, class action treatment allows injured persons the ability to seek redress on claims that might be impracticable to pursue individually.

XI. CLAIM FOR RELIEF
MONOPOLIZATION IN VIOLATION OF SECTION 2 OF THE SHERMAN ACT

124. Uniondale Chemists repeats, and incorporates by reference, the allegations in the preceding paragraphs.

125. Astellas used willful and exclusionary means as part of an overall scheme described herein to improperly maintain and extend its monopoly power in the tacrolimus market. Astellas accomplished this scheme by filing a baseless citizen petition with the FDA in an attempt to delay generic versions of Prograf from entering the market.

126. The goal, purpose, and effect of Astellas' scheme was to prevent, delay, and/or minimize the success of the entry of AB-rated generic tacrolimus competitors which would have sold generic tacrolimus capsules in the United States at prices significantly below Astellas' prices for Prograf, thereby effectively causing the average market price of tacrolimus to decline dramatically and cause Astellas' sales of Prograf to fall.

127. The goal, purpose, and effect of Astellas' scheme was also to maintain and extend its monopoly power with respect to tacrolimus. Astellas' illegal scheme enabled Astellas to continue charging supra-competitive prices for tacrolimus, without a substantial loss of sales, reaping substantial unlawful monopoly profits.

128. Astellas' actions acted as a fraud on the FDA, which reasonably relied on Astellas to make legitimate and objective arguments in its petition. Because Astellas failed to provide unbiased information, the FDA, relying on Astellas to be presenting serious issues, spent more time than necessary and more time than it otherwise would have investigating and responding to the petition.

129. Uniondale Chemists and members of the Class purchased substantial amounts of Prograf directly from Astellas.

130. As a result of Astellas' illegal conduct, Plaintiff and members of the Class were compelled to pay, and did pay, more than they would have paid for tacrolimus absent Astellas' illegal conduct. But for Astellas' illegal conduct, competitors would have begun marketing generic versions of Prograf well before they actually did.

131. Had generic manufacturers of tacrolimus entered the market and lawfully competed with Astellas in a timely fashion, Plaintiff and other members of the Class would have substituted lower-priced generic tacrolimus for the higher-priced brand name Prograf for some or all of their tacrolimus requirements, and/or would have paid lower net prices on their remaining Prograf purchases.

132. As a consequence, Uniondale Chemists and the Class have sustained damage to their business and property in the form of overcharges. The injury to Plaintiff and the Class is the type of injury antitrust laws were designed to prevent, and the injury flows from Astellas ' unlawful conduct

133. Astellas' scheme was in the aggregate an act of monopolization of the market for tacrolimus in the United States, in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2.

WHEREFORE, Plaintiff, on behalf of itself and the Class respectfully, requests that:

a. The Court determine that this action may be maintained as a class action pursuant to Rule 23 of the Federal Rules of Civil Procedure, and direct that reasonable notice of this action, as provided by Rule 23(c)(2) of the Federal Rules of Procedure, be given to the Class;

b. The acts alleged herein be adjudged and decreed to be unlawful and willful acts of monopolization in restraint of trade in violation of Section 2 of the Sherman Act, 15 U.S.C. § 2;

c. The Class be awarded treble the damages determined to have been sustained by the Class, and that judgment be entered against Defendant in favor of the Class;

d. The Class recover their costs of suit, including reasonable attorneys' fees as provided by law; and

e. The Class be granted such other, further and different relief as the nature of the case may require or as may be determined to be just, equitable, and proper by this Court.

Dated: April 20, 2011

Plaintiff,

By:*/s/ Marvin A. Miller*

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JURY DEMAND

Pursuant to Fed. R. Civ. P. 38(b), Plaintiff demands a trial by jury.

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